noted at the time of valve replacement, therefore making the procedure technically more difficult.

As noted above, the severity of the bone disease and the severity of the valvular disease are not necessarily concordant. Intuitively, one might expect that in patients with osteogenesis imperfecta and many fractures, more severe cardiovascular pathologic conditions might develop than in those who have had fewer fractures. However, it is evident from Table 1 that severe aortic regurgitation can occur in patients with fewer fractures. Conversely, patients with many fractures may have only mild aortic regurgitation. Age seems to have little effect on the severity of valvular lesions. We conclude that in patients with all degrees of osteogenesis imperfecta, severe cardiovascular abnormalities can develop which affect the aortic root and valve more frequently than the mitral valve. Valve replacement is technically feasible, and the clinical results are satisfactory in such cases.

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Poisoning Involving Improperly Stored Parathion

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PESTICIDES, especially of the highly toxic organophosphate variety, are prominent among causes of poisoning in children. Many of these cases involve transfer of the pesticide from its original container into a container a child associates with food and drink; or improper storage allowing a child ready access to the pesticide.[1-3] This report describes a recent case of the latter kind involving parathion and illustrates a cooperative effort between a physician and an analytical laboratory with pesticide and pesticide metabolite analytical capability. Exposure history, diagnosis, treatment and excretion of metabolites are presented.

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Report of a Case

A 4-year-old girl, sleeping with her mother, awakened at about 3 AM with some respiratory distress and a low-grade fever. The girl's mother, thinking that a recent cold with fever and vomiting had returned, gave her aspirin. The child made her way back to her own bed and the mother noticed that the little girl was wobbly on her feet. The mother heard nothing further from her during the night. At 9 AM she went to see why the child had not wakened and found her comatose, febrile and having a great deal of trouble breathing. An ambulance was called and the child was taken immediately to a local hospital.

On admission the patient was comatose and unresponsive to stimulation by pinprick or pinching. Rectal temperature was 39.2°C (102.6°F), pulse was 120 and regular and respiration was 52 and labored. Muscular twitching involving the face, neck and upper extremities was noted. There was no evidence of head trauma or other physical injury. Examination of the patient's eyes showed pinpoint, equal and round pupils which were unresponsive to light or accommodation. A gross vertical nystagmus was also present. Findings on examination of the ears were normal. Copious mucousy oral secretions were noted with no evidence of intraoral trauma. Rhinorrhea was also noted. The patient's neck was supple, with

no apparent discomfort on motion. No adenopathy was noted.

Examination of the chest showed there to be increased inspiratory effort throughout. Coarse rhonchi were scattered throughout with no rales. Cardiac examination showed a pronounced sinus tachycardia with a rate of 120 and no gross murmurs.

The abdomen was soft with diminished bowel sounds, and an obviously distended bladder extending up to the umbilicus was noted. The bladder was catheterized. The genitalia were normal.

Deep tendon reflexes were symmetrically depressed. Toes were down going.

While the examination was proceeding, ambulance personnel were examining the patient's homesite where they noted that a paper sack of 25 percent wettable powdered parathion had fallen to the ground in an adjacent garage and broken. The patient and her brother and sister had been playing in the powder. With this information, and clinical features consistent with organophosphate poisoning, 1 mg of atropine was given intravenously. The patient immediately became calmer, and began to breathe more easily, the copious secretions diminished and she became semiresponsive. Her pupils remained pinpoint, however, and in 20 to 30 minutes she began to slip back into a comatose state. A second milligram of atropine was then given intravenously and good improvement was again noted but with residual muscular tremors. On advice of a toxicologist 0.5 gram of pralidoxime chloride (Protopam Chloride®) was given slowly over 1½ hours. Immediate improvement was noted and, with the exception of some drowsiness, the patient was asymptomatic by 12:30 PM. She was released from the hospital five days after admission. The mother was contacted two weeks after the precipitating incident and she reported that no further problems were experienced by the child.

Laboratory Findings

Samples of blood, urine and gastric washings were taken. The blood was separated into plasma and red blood cells and analyzed, respectively, for pseudocholinesterase and acetyl cholinesterase activity using the pH Stat method which is a continuous automatic titration of the acetic acid formed by the action of cholinesterase on acetyl choline substrate at constant temperature. Enzyme activity is expressed as micromoles of substrate hydrolyzed per minute per ml of sample.

Cholinesterase values show the typical prompt response to treatment with pralidoxime chloride (Protopam® Chloride) of organophosphate poisoning. These results are shown in Table 1.

The two principal metabolic pathways for parathion in the human are shown in Figure 1. Both parathion and its oxidation product paraoxon are powerful cholinesterase inhibitors.

Exposure to parathion can thus be confirmed by analysis of urine for the end metabolic products shown: diethyl thiophosphoric acid (DETP), diethyl phosphoric acid (DEP) and p-nitrophenol (PNP). Accordingly, a specimen of the patient's urine was analyzed for DEP and DETP by the method of Shafik and co-workers[4] and for PNP by the method of Cranmer and co-workers.[5] Results of the analysis are shown in Table 2.

Examination of the table shows steadily declining values of DETP. Values for PNP, however, show a second peak in the samples taken on May 23 and May 24. A similar pattern appears to hold for the DEP excretion. These are shown graphically in Figure 2.

Much the same pattern of PNP excretion was reported by Arterberry and associates in 1961.[6] No analysis for DEP was possible at that time.

Gastric washings were negative for ethyl parathion. This is possibly due to the exposure being primarily dermal although some ingestion had apparently also occurred. The possibility also exists that the period of several hours from the last possible ingestion to admission to the hospital may have been long enough to allow the pesticide to clear the stomach.

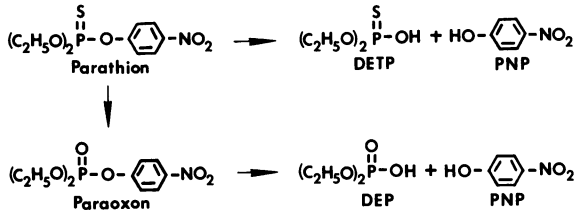

Figure 1.—Metabolism of parathion. DETP = diethyl thiophosphoric acid, DEP = diethyl phosphoric acid, PNP = p-nitrophenol.

TABLE 1.—*Serial Cholinesterase Determinations*

	Micromoles/minute-ml	
	Plasma	*Red Blood Cells*
5/21 Before Protopam	0.21	0.95
5/21 After Protopam	0.52	6.18
5/22 24 hours after Protopam ..	0.72	6.54

Normal Adult Values: Plasma = 2.4-6.6; RBC = 12.0-16.7

Discussion

In retrospect, it appears that the illness suffered by this child two days before the poisoning episode was likely a mild poisoning. The two other children, in whom symptoms did not develop, had also been playing in the parathion powder. Their exposure was evidently only dermal and their evening bath probably prevented the development of clinical symptoms. The patient had also been bathed and the bathing probably prevented a much more serious poisoning.

This poisoning follows an altogether too typical pattern of pesticide poisoning in children. Improper storage of highly toxic materials, allowing access by children, is clearly the cause of this episode. These preventable poisonings will likely become more common as the organophosphate and carbamate pesticides replace the increasingly banned, but generally less toxic, chlorinated compounds unless a strong public education program is mounted relative to proper storage and handling of pesticide materials. It also appears to be essential that practicing physicians become acquainted with the symptoms of this type of poisoning so that prompt diagnosis may be made and appropriate treatment may be started as soon as possible.

Although is is beyond the scope of this report to present a detailed description of differential diagnosis and treatment of organophosphate poisonings, it is appropriate to summarize the principal clinical symptoms of various degrees of poisoning by organophosphate compounds.

- *Mild poisoning:* anorexia, headache, dizziness, weakness, anxiety, tremors of tongue and eyelids, miosis, impairment of visual acuity.
- *Moderate poisoning:* nausea, salivation, lacrimation, abdominal cramps, vomiting, sweating, slow pulse, muscular tremor.
- *Severe poisoning:* diarrhea, pinpoint and nonreactive pupils, respiratory difficulty, pulmonary edema, cyanosis, loss of sphincter control, convulsions, coma, heart block.

Exposure routes may be oral, dermal or by inhalation, and symptoms generally appear within half an hour to three hours after exposure, but rarely beyond 12 hours.

Confirmation of the diagnosis of organophosphate insecticide poisoning may be made by the laboratory tests described in this report.

Detailed discussions of the pharmacology and toxicology of pesticides may be found in several references.[7-10]

TABLE 2.—*Analysis of Urine*

Date	Time	Values in Parts per Million DETP	DEP	PNP
5/21/75	?	3.88	0.47	3.76
5/22/75	2:00 pm	0.72	0.30	0.89
5/23/75	1:10 pm	0.37	0.35	1.37
5/24/75	8:00 am	0.19	0.27	1.32
5/25/75	8:00 am	0.19	0.15	0.55
5/26/75	7:30 pm	0.11	0.07	0.26

DETP = diethyl triophosphoric acid
DEP = diethyl phosphoric acid
PNP = p-nitrophenol

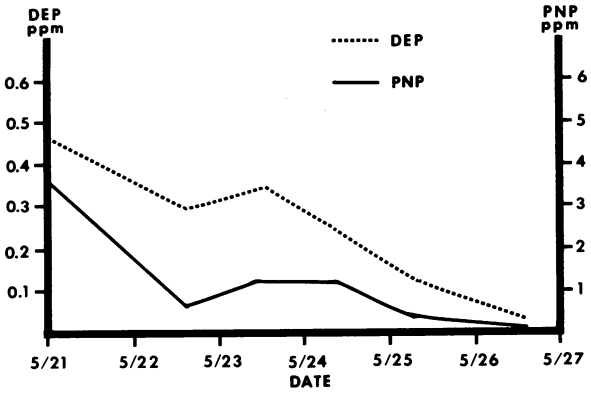

Figure 2.—Urine analysis. DEP = diethyl phosphoric acid, PNP = p-nitrophenol.

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